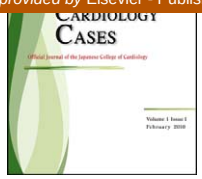
Journal of Cardiology Cases (2011) 3, e71–e74

journal homepage: www.elsevier.com/locate/jccase



Case Report

A patient with Wegener's granulomatosis in apparent remission presenting with complete atrioventricular block

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Received 7 November 2010; received in revised form 16 January 2011; accepted 24 January 2011

KEYWORDS
Wegener's granulomatosis;
Complete atrioventricular block;
Cardiac involvement;
Multisystem disorder;
Pacemaker

Summary Wegener's granulomatosis is a systemic necrotizing granulomatous vasculitis of small- to medium-sized vessels typically affecting upper and lower airways, lungs, and kidneys. Cardiac involvement is less common and conducting tissue involvement is extremely rare. Cardiac manifestations are often not clinically apparent, but are associated with increased mortality. We report the case of a 36-year-old female with Wegener's thought to be in remission, presenting in complete atrioventricular (AV) block, with echocardiographic evidence of basal interatrial septum and basal lateral left atrial wall thickening. Despite immunosuppression therapy a permanent pacemaker was required for recurring complete AV block. Although rare, this case emphasizes the need for careful and regular screening for cardiac involvement in this multi-system condition.

Introduction

Wegener's granulomatosis is a systemic necrotizing granulomatous vasculitis of small- to medium-sized vessels associated with diffuse cytoplasmic anti-neutrophil cytoplasmic antibodies (cANCA) specific for proteinase-3 (PR3). It typically affects the upper and lower airways, lungs, and kidneys. Less commonly, cardiac involvement manifests in 6–25% of unselected patients with Wegener's granulomatosis, and up to 44% of patients with severe renal involvement, usually as pericarditis, myocarditis, and aortitis, although myocardial infarction is also recognized [1]. Cardiac conducting tissue involvement is extremely rare. Although often not clinically apparent, cardiac involvement is associated with increased mortality [2]. We report a case of complete atrioventricular block in a patient with Wegener's granulomatosis thought to be in remission, and review the current literature.

Case report

A 36-year-old woman with a three-month history of pre-syncopal symptoms presented with two syncopal episodes

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1878-5409/$ – see front matter
doi:10.1016/j.jccase.2011.01.008

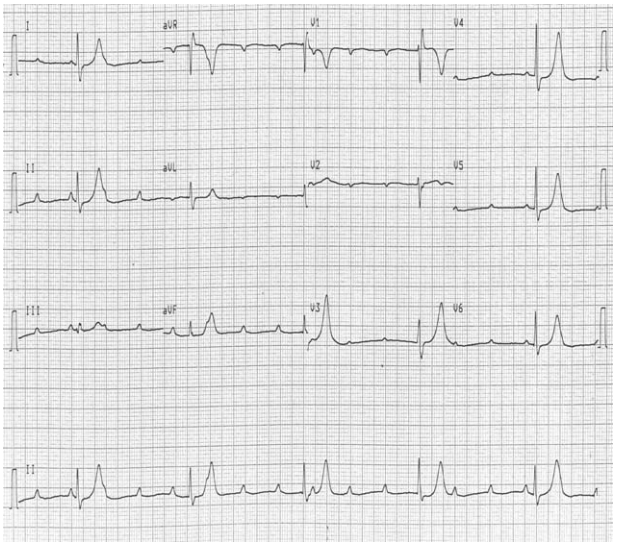

Figure 1 Electrocardiogram showing complete atrioventricular block.

in May 2010. At the initial presentation her electrocardiogram showed sinus rhythm with first degree atrioventricular (AV) block and a PR interval of 250 ms. Overnight monitoring did not reveal any other abnormality and she was discharged with plans for further outpatient cardiac investigation. Six days later she re-presented with a second episode of syncope and at this time electrocardiogram showed complete AV dissociation with a ventricular rate of 28 beats per minute (Fig. 1). No other symptoms or signs of systemic illness were elicited.

In June 2008 she had been diagnosed with Wegener's granulomatosis after presenting with a two-week history of nasal crusting, loss of hearing, polyarthralgia, and small-vessel ischemia of the fingers and toes. At that time erythrocyte sedimentation rate (ESR) was 86 mm/h, C-reactive protein (CRP) 140 mg/l, and cANCA immunofluorescence was positive with anti-PR3 titre of 103 units (normal range 0—7 units) by enzyme-linked immunosorbent assay. An electrocardiogram had been performed showing sinus rhythm with a normal PR interval and QRS duration, but regrettably no other cardiac investigation, including echocardiography, had been undertaken at the time of first diagnosis. She was treated with high-dose steroids, cyclophosphamide, prostacyclin, and co-trimoxazole. Clinical and laboratory remission was achieved by September 2008, and she was maintained on azathioprine therapy.

At the time of this admission, her inflammatory markers were mildly elevated (ESR of 19 mm/h and CRP of 23 mg/l) and the anti-PR3 titre was normal (4.5 units). Serum potassium was increased at 7 mmol/l with a creatinine of 118 μmol/l, without erythrocyturia, urinary casts, or proteinuria. Although she initially settled into a sinus rhythm with first-degree AV block following correction of her hyperkalaemia, complete AV block recurred the next day despite normal electrolyte levels.

A transthoracic echocardiogram showed markedly thickened basal segments of her left atrium, including the basal interatrial septum (Figs. 2 and 3). Left ventricular chamber size and wall thickness were normal, with normal systolic

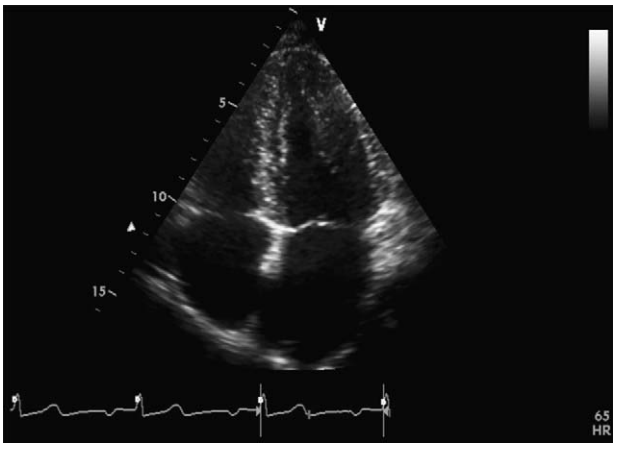

Figure 2 Transthoracic apical 4-chamber view showing marked thickening of the basal interatrial septum and basal lateral atrial wall.

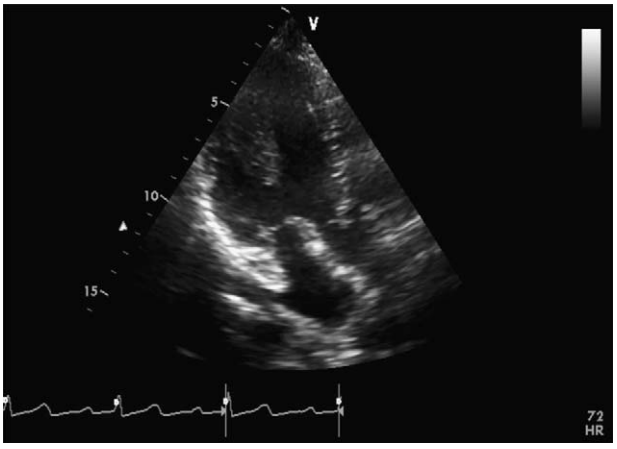

Figure 3 Transthoracic apical 3-chamber view showing similar marked thickening of the basal posterior and anterior left atrial wall.

and diastolic function. It was felt, given the raised inflammatory markers, that she may have active granulomatous disease affecting the region of the atrioventricular node and she was treated with intravenous methylprednisolone and cyclophosphamide. Despite this, she continued to experience symptomatic high-grade AV block with prolonged episodes of ventricular standstill and so a dual chamber pacemaker was implanted.

At three-month follow-up she remained asymptomatic. However, her transthoracic echocardiographic appearances were essentially unchanged and she had been pacing dependent for 85% of the time in the month up to review.

Discussion

Cardiac involvement of Wegeners's granulomatosis was first reported by Wegener in 1936, but the first case of associated complete AV block did not appear until 1969 [3]. Since then, there have only been 13 cases previously reported in the published literature and all but one case was associated with systemic disease (Table 1) [1,3—14]. Complete AV block was present at disease onset in 50% and in 70% by one year. Half

Table 1 Summary of reported cases of complete heart block.

Case	Authors	Year	Age/sex	Type	Duration (months)	Previous treatment	Treatment	Outcome
1	Longauer [3]	1969	47, F	syst	0	—	cs, ppm	died
2	Forstot [1]	1980	26, M	syst	11	cs	cs, cyc, tpw, ppm	resolution
3	Krulder [5]	1985	46, M	syst	12	—	cs, cyc, ppm	resolution
4	Schiavone [6]	1985	43, M	syst	7	—	cs, cyc	resolution
5	Handa [7]	1997	35, M	syst	0	—	cs, cyc, tpw	resolution
6	Ohkawa [4]	1999	61, F	syst	0	—	cs	died
7	Khurana [8]	2000	47, F	syst	1	—	cs, cyc	resolution
8	Suleymenlar [9]	2002	27, F	syst	13	cs, cyc	cs, cyc, tpw	resolution
9	Wilcke [10]	2003	63, M	syst	0.3	—	cs, cyc, pph, tpw	resolution
10	Ghaussy [11]	2004	36, M	lim	>12	—	—	resolution
11	Elikowski [12]	2006	52, M	syst	14	cs, cyc, cic	cs, cyc, tpw, ppm	unknown
12	Lim [13]	2007	61, M	syst	2	—	cs, cyc	resolution
13	Sarlon [14]	2010	77, M	syst	0	—	cs, cyc, ppm	died

Abbreviations used: F, female; M, male; lim, limited; syst, systemic; cs, corticosteroids; cyc, cyclophosphamide; cic, ciclosporin; aza, azathioprine; ppm, permanent pacemaker; tpw, temporary pacing wire.

the cases were asymptomatic, although all had clinical or laboratory evidence of active disease.

Echocardiograms were performed in nine of the patients and abnormalities were present in six; most commonly valvular abnormalities and pericardial effusion. This is in keeping with a review of echocardiography in 85 patients with confirmed Wegener's granulomatosis finding abnormalities in 86% [2]. Treatment included corticosteroids, cyclophosphamide, temporary pacing wire, and pacemaker implantation. The complete AV block resolved in 9 of the 13 cases. Two patients died of cardiac dysrhythmia, neither of which had been treated with cyclophosphamide. Postmortem examination of the first case reported by Longauer et al. showed granulomatous involvement of the conduction system with fibrosis and hyalinization, but not necrosis [3]. In the second case, Ohkawa et al. reported small foci of inflammation affecting the sinus and AV nodes with AV nodal arteritis, inflammatory necrotising granulomatous involvement of the conducting system, and myocardium associated with an exudative endocarditis and fibrinous pericarditis [4].

Compared to previously published cases, our patient was unusual in that she had relatively longer disease duration of 24 months at diagnosis, she had previously been treated with intravenous cyclophosphamide, and she had no clinical or laboratory evidence of extra-cardiac increased disease activity. Although a low level cANCA level was detected in our patient, this would be considered as normal according to local reference values. The significance of this is unclear as some Wegner's patients experience persistent detectability of cANCA without adverse outcome, whilst up to 20% of patients with limited active disease may have negative levels [15,16]. Given this uncertainty, we opted to treat her with further immunosuppression on the basis of raised inflammatory markers and cardiac imaging suspicious for granulomatous involvement. However, it is certainly possible that her echocardiographic appearances represented fibrosis rather than active granulomatous disease. The unchanged appearance at follow up may support the latter possibility. On the transthoracic images presented the obvious thickening is of the atrial walls which would not in itself lead to complete AV block, however, she is young and otherwise well and so we would feel that an association between these abnormalities and her presentation is likely. We had hoped to arrange magnetic resonance imaging to try and clarify if disease was also present at the AV node and His conducting tissue, but her need for pacing support prevented this.

In summary, complete AV block is a rare but treatable manifestation of cardiac involvement usually associated with early active systemic disease. All patients diagnosed with Wegener's granulomatosis should be screened with a baseline electrocardiogram and a transthoracic echocardiogram to document cardiac involvement and alert clinicians to those at risk of further cardiac complications. Echocardiography frequently detects abnormalities suggesting cardiac involvement in asymptomatic individuals and this case highlights that later presentation of cardiac abnormalities than previously reported can occur and lifelong surveillance needs to be considered given the poorer prognosis in these individuals. In turn, all patients presenting with cardiac abnormalities and evidence of systemic inflammation should be screened for Wegener's by clinical, laboratory, and radiographic assessment.

References

[1] Forstot JZ, Overlie PA, Neufeld GK, Harmon CE, Forstot SL. Cardiac complications of Wegener granulomatosis: a case report of complete heart block and review of the literature. Semin Arthritis Rheum 1980;10:148—54.

[2] Oliveira GH, Seward JB, Tsang TS, Sprecks U. Echocardiographic findings in patients with Wegener granulomatosis. Mayo Clin Proc 2005;80:1435—40.

[3] Longauer F, Takac M, Halasova K. On damage of the heart conduction system in Wegener's granulomatosis. Z Kreislaufforsch 1969;58:412—21.

[4] Ohkawa S, Miyao M, Chida K, Mizuuchi T, Kida K, Takubo K, Ohtsubo K. Extensive involvement of the myocardium and the cardiac conduction system in a case of Wegener's granulomatosis. Jpn Heart J 1999;40:509—15.

[5] Krulder JW, Niermeijer P. Reversible atrioventricular block due to Wegener's granulomatosis. Neth J Med 1985;28:28—31.

[6] Schiavone WA, Ahmad M, Ockner SA. Unusual cardiac complications of Wegener's granulomatosis. Chest 1985;88: 745—8.
[7] Handa R, Wali JP, Aggarwal P, Wig N, Biswas A, Kumar AK. Wegener's granulomatosis with complete heart block. Clin Exp Rheumatol 1997;15:97—9.
[8] Khurana C, Mazzone P, Mandell B. New onset left bundle branch block with right axis deviation in a patient with Wegener's granulomatosis. J Electrocardiol 2000;33: 199—201.
[9] Suleymenlar G, Sarikaya M, Sari R, Tuncer M, Sevinc A. Complete heart block in a patient with Wegener's granulomatosis in remission—a case report. Angiology 2002;53: 337—40.
[10] Wilcke JT, Nielsen PK, Jacobsen TN. Reversible complete heart block due to Wegener's granulomatosis. Int J Cardiol 2003;89:297—8.
[11] Ghaussy NO, Du Clos TW, Ashley PA. Limited Wegener's granulomatosis presenting with complete heart block. Scand J Rheumatol 2004;33:115—8.
[12] Elikowski W, Baszko A, Puszczewicz M, Stachura E. Complete heart block due to Wegener's granulomatosis: a case report and literature review. Kardiol Pol 2006;64:622—7.
[13] Lim HE, Lee YH, Ahn JC. Wegener's granulomatosis with progressive conduction disturbances and atrial fibrillation. Heart 2007;93:77.
[14] Sarlon G, Durant C, Grandgeorge Y, Bernit E, Veit V, Hamidou M, Schleinitz N, Harlé JR. Cardiac involvement in Wegener's granulomatosis: report of four cases and review of the literature. Rev Med Interne 2010;31:135—9 [in French].
[15] Witko-Sarsat V, Reuter N, Mouthon L. Interaction of proteinase 3 with its associated partners: implications in the pathogenesis of Wegener's granulomatosis. Curr Opin Rheumatol 2010;22:1—7.
[16] Finkielman JD, Lee AS, Hummel AM, Viss MA, Jacob GL, Homburger HA, Peikert T, Hoffman GS, Merkel PA, Spiera R, St Clair EW, Davis Jr JC, McCune WJ, Tibbs AK, Ytterberg SR, et al. ANCA are detectable in nearly all patients with active severe Wegener's granulomatosis. Am J Med 2007;120, 643. e9—14.